PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
DK62208PC		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP2004/011632	15/10/2004	17/10/2003
Applicant		
DKFZ DEUTSCHES KREBSFORSCHUNGSZENTRUM...		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 16 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
      [ ] The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. [X] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (See Box II).

3. [X] **Unity of invention is lacking** (see Box III).

4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant.
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant.
   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      [ ] as suggested by the applicant.
      [ ] as selected by this Authority, because the applicant failed to suggest a figure.
      [ ] as selected by this Authority, because this figure better characterizes the invention.
   b. [X] none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/011632

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material

   [X] a sequence listing

   [ ] table(s) related to the sequence listing

   b. format of material

   [X] in written format

   [X] in computer readable form

   c. time of filing/furnishing

   [X] contained in the international application as filed

   [X] filed together with the international application in computer readable form

   [ ] furnished subsequently to this Authority for the purpose of search

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/011632

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1, 6-8, 18, 19, 24 (completely); 4, 9-10, 10-17, 24 (partially)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1, 4 in part, 6-8, 9-10 in part, 13-17 in part, 18, 19, 24 in part

Use of ADAM 12 protein or a nucleic acid molecule comprising a nucleic acid with a sequence of ADAM 12 for diagnosis of preeclampsia or a related syndrome; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a nucleic acid molecule comprising a nucleic acid with a sequence of ADAM 12, and ii) detecting the binding of the nucleic acid; or the use of a nucleic acid molecule comprising a nucleic acid with a sequence of ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a nucleic acid molecule comprising a nucleic acid with a sequence of ADAM 12; or use of a nucleic acid molecule with a sequence of ADAM 12 for the manufacture of a medicament for the treatment of preeclampsia or a related syndrome.

---

2. claims: 2-5 in part, 9-10 in part, 11, 12, 13-17 in part, 20-28 in part

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12; or use of an inhibitor of the biological activity ADAM 12 for the manufacture of a medicament for the treatment of preeclampsia or a related syndrome; or use of ADAM 12 for the identification of an inhibitor of ADAM 12;
a method for identification of an inhibitor of the biological activity of ADAM 12 comprising: i) contacting ADAM 12 with a suitable substrate, and ii) measuring the decrease in processing of the substrate in the presence as compared to the absence of a candidate for an inhibitor molecule; a method for the preparation of a pharmaceutical composition wherein an inhibitor of ADAM 12 synthesized in adequate amounts, and formulated into a pharmaceutical composition. Wherein the ligand or inhibitor is a disintegrin domain metalloproteinase inhibitors, in particular KB-R7785 or a derivative thereof.

---

3. claims: 2-5 in part, 9-17 in part, 20-28 in part

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12; or use of an inhibitor of the biological activity ADAM 12 for the manufacture of a medicament for the treatment of preeclampsia or a related syndrome; or use of ADAM 12 for the identification of an inhibitor of ADAM 12;
a method for identification of an inhibitor of the biological activity of ADAM 12 comprising: i) contacting ADAM 12 with a suitable substrate, and ii) measuring the decrease in processing of the substrate in the presence as compared to the absence of a candidate for an inhibitor molecule; a method for the preparation of a pharmaceutical composition wherein an inhibitor of ADAM 12 synthesized in adequate amounts, and formulated into a pharmaceutical composition. Wherein the ligand or inhibitor is a TIMP, in particular TIMP-1, TIMP-2, or TIMP-3.

---

4. claims: 2-5 in part, 9-17 in part, 20 in part, 21 in part, 23-28 in part

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12.
Wherein the ligand is IGFBP-3 or IGFBP-5.

---

5. claims: 2-5 in part, 9-17 in part, 20 in part, 21 in part, 23-28 in part

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12.
Wherein the ligand is HB-EGF.

---

6. claims: 2-5 in part, 9-17 in part, 20-28 in part

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12; or use of an inhibitor of the biological activity ADAM 12 for the manufacture of a medicament for the treatment of preeclampsia or a related syndrome; or use of ADAM 12 for the identification of an inhibitor of ADAM 12;
a method for identification of an inhibitor of the biological activity of ADAM 12 comprising: i) contacting ADAM 12 with a suitable substrate, and ii) measuring the decrease in processing of the substrate in the presence as compared to the absence of a candidate for an inhibitor molecule; a method for the preparation of a pharmaceutical composition wherein an inhibitor of ADAM 12 synthesized in adequate amounts, and formulated into a pharmaceutical composition. Wherein the ligand or inhibitor is alpha2-macroglobulin.

---

7. claims: 2-5 in part, 9-17 in part, 20 in part, 21 in part, 23-28 in part

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12.
Wherein the ligand is PKC-delta.

---

8. claims: 2-5 in part, 9-17 in part, 20 in part, 21 in part, 23-28 in part

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12.
Wherein the ligand is alpha-actinin or alpha-actinin-2.

---

9. claims: 2-5 in part, 9-17 in part, 20 in part, 21 in part, 23-28 in part

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12.
Wherein the ligand is src.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

---

10. claims: 2-5 in part, 9-17 in part, 20 in part, 21 in part, 23-28 in part

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12.
Wherein the ligand is Grb-2.

---

11. claims: 2-5 in part, 9-17 in part, 20 in part, 21 in part, 23-28 in part

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12.
Wherein the ligand is syndecan-4.

---

12. claims: 2-5 in part, 9-17 in part, 20-28 in part

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12; or use of an inhibitor of the biological activity ADAM 12 for the manufacture of a medicament for the treatment of preeclampsia or a related syndrome; or use of ADAM 12 for the identification of an inhibitor of ADAM 12;
a method for identification of an inhibitor of the biological activity of ADAM 12 comprising: i) contacting ADAM 12 with a suitable substrate, and ii) measuring the decrease in processing of the substrate in the presence as compared to the absence of a candidate for an inhibitor molecule; a method for the preparation of a pharmaceutical composition wherein an inhibitor of ADAM 12 synthesized in adequate amounts, and formulated into a pharmaceutical composition. Wherein the ligand or inhibitor is an antibody, or the ligand is a nucleic acid or protein aptamer.

---

13. claims: 2-5 in part, 9-17 in part, 20 in part, 21 in part, 23-28 in part

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12; or use of an inhibitor of the biological activity ADAM 12 for the manufacture of a medicament for the treatment of preeclampsia or a related syndrome; or use of ADAM 12 for the identification of an inhibitor of ADAM 12;
a method for identification of an inhibitor of the biological activity of ADAM 12 comprising: i) contacting ADAM 12 with a suitable substrate, and ii) measuring the decrease in processing of the substrate in the presence as compared to the absence of a candidate for an inhibitor molecule; a method for the preparation of a pharmaceutical composition wherein an inhibitor of ADAM 12 synthesized in adequate amounts, and formulated into a pharmaceutical composition.
Wherein the ligand or inhibitor is P-LAP.

---

14. claims: 2-5 in part, 9-17 in part, 20 in part, 21 in part, 23-28 in part

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of a ligand binding specifically to ADAM 12 for diagnosis of preeclampsia or related syndrome; or a method for the identification of ligands binding specifically to ADAM 12 comprising contacting ADAM 12 with at least one candidate for a ligand, and ii) measuring the binding of the candidate for a ligand to ADAM 12; or a method for diagnosis of preeclampsia or a related syndrome comprising: i) bringing a biopsy or bodily fluid sample in contact with a specifically binding ligand to ADAM 12 and ii) detecting the binding of ligand;
or the use of a ligand binding to ADAM 12 for the manufacture of a diagnostic for the diagnosis of preeclampsia or a related syndrome; or a diagnostic or a diagnostic kit containing a ligand binding to ADAM 12; or use of an inhibitor of the biological activity ADAM 12 for the manufacture of a medicament for the treatment of preeclampsia or a related syndrome; or use of ADAM 12 for the identification of an inhibitor of ADAM 12;
a method for identification of an inhibitor of the biological activity of ADAM 12 comprising: i) contacting ADAM 12 with a suitable substrate, and ii) measuring the decrease in processing of the substrate in the presence as compared to the absence of a candidate for an inhibitor molecule; a method for the preparation of a pharmaceutical composition wherein an inhibitor of ADAM 12 synthesized in adequate amounts, and formulated into a pharmaceutical composition.
Wherein the ligand or inhibitor is not comprised in the above-mentioned subjects 1-13.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/011632

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/68 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, MEDLINE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X D1	GILPIN B J ET AL: "A novel, secreted form of human ADAM 12 (Meltrin alpha) provokes myogenesis in vivo" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 273, no. 1, 2 January 1998 (1998-01-02), pages 157-166, XP002229017 ISSN: 0021-9258 cited in the application	15-17
Y	page 157, left-hand column, line 1 page 157, right-hand column, last paragraph - page 158, left-hand column, paragraph 1 page 165, left-hand column, paragraph 2 ----- -/--	1,4, 6-10,13, 14

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 January 2005	01 04 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Marttin, E

3

Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X D4	WO 03/020220 A (PROCACCIO VINCENT ; WALLACE DOUGLAS C (US); KERSTANN KEITH (US); LEVY) 13 March 2003 (2003-03-13) claim 2; sequence 290	15-17
Y D2	KOLBEN M ET AL: "Proteases and their inhibitors are indicative in gestational disease." EUROPEAN JOURNAL OF OBSTETRICS, GYNECOLOGY, AND REPRODUCTIVE BIOLOGY. IRELAND SEP 1996, vol. 68, no. 1-2, September 1996 (1996-09), pages 59-65, XP002272282 ISSN: 0301-2115 page 63, left-hand column, line 12 - line 15 page 64, left-hand column, line 23 - line 25 page 64, left-hand column, line 43 - line 49	1,4, 6-10,13, 14
Y D3	US 2003/170627 A1 (WONG SOPHIA LI-MING ET AL) 11 September 2003 (2003-09-11)	1,4, 6-10,13, 14
A	page 1, paragraph 3 - paragraph 5 page 4, paragraph 45 page 10, paragraph 111 page 11, paragraph 118	15-19,24
Y D2	MASANORI ASAKURA ET AL: "Cardiac hypertrophy is inhibited by antagonism of ADAM12 processing of HB- EGF: Metalloproteinase inhibitors as a new therapy" NATURE MEDICINE, NATURE AMERICA, NEW YORK, US, vol. 8, no. 1, January 2002 (2002-01), pages 35-40, XP002965243 ISSN: 1078-8956	1,4, 6-10,13, 14
A	page 35, right-hand column, line 8 - line 9	15-19,24
Y D9	PANG Z J ET AL: "Expression profile of trophoblast invasion-associated genes in the pre-eclamptic placenta." BRITISH JOURNAL OF BIOMEDICAL SCIENCE. ENGLAND 2003, vol. 60, no. 2, September 2003 (2003-09), pages 97-101, XP002272487 ISSN: 0967-4845 the whole document	1,4, 6-10,13, 14

-/--

3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/011632

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE WPI Section Ch, Week 198715 Derwent Publications Ltd., London, GB; Class B04, AN 1987-106528 XP002272283 & SU 1 250 257 A (MOSC SECOND MED INS) 15 August 1986 (1986-08-15) abstract	1,4, 6-10, 13-19,24
A	WO 99/46597 A (DIAGNOSTIC SYSTEMS LAB INC) 16 September 1999 (1999-09-16) page 8, line 22 - page 9, line 2; claims 17,18; example 5	1,4, 6-10, 13-19,24
A	LEACH R E ET AL: "Pre-eclampsia and expression of heparin-binding EGF-like growth factor" LANCET, XX, XX, vol. 360, no. 9341, 19 October 2002 (2002-10-19), pages 1215-1219, XP004388635 ISSN: 0140-6736 page 1218, left-hand column, line 13 - right-hand column, line 22	1,4, 6-10, 13-19,24
P,X	US 2004/002467 A1 (DOBIE KENNETH W ET AL) 1 January 2004 (2004-01-01) paragraphs [0010] - [0015], [0031]	15,16

3

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP2004/011632

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03020220 A	13-03-2003	CA 2459061 A1	13-03-2003
		EP 1432823 A2	30-06-2004
		WO 03020220 A2	13-03-2003
		CA 2356540 A1	28-02-2003
US 2003170627 A1	11-09-2003	NONE	
SU 1250257 A	15-08-1986	SU 1250257 A1	15-08-1986
WO 9946597 A	16-09-1999	US 6248546 B1	19-06-2001
		AU 760099 B2	08-05-2003
		AU 2996599 A	27-09-1999
		CA 2323450 A1	16-09-1999
		EP 1070255 A1	24-01-2001
		NZ 507400 A	29-08-2003
		RU 2206897 C2	20-06-2003
		WO 9946597 A1	16-09-1999
US 2004002467 A1	01-01-2004	NONE	